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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/046,833	03/24/1998	DAKAI LIU	ENZ-56(DIV4)	2594
28169	7590	01/29/2004	EXAMINER	
ENZO THERAPEUTICS, INC. C/O ENZO BIOCHEM INC. 527 MADISON AVENUE 9TH FLOOR NEW YORK, NY 10022			GUZO, DAVID	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/046,833

Applicant(s)

LIU ET AL.

Examiner

David Guzo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 75-90 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 75-90 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/24/03 has been entered.

The following is noted concerning the format of the claims presented in the response filed 10/24/03. Claims 75-90 were listed as "NEW" claims. This is incorrect, these claims have been pending since **3/15/02** and cannot be listed as "NEW". Also, the claims presented 10/24/03 appear to contain amendments to claims 75 and 88-90 which applicants attempted to enter in an After Final amendment. The After Final amendment was not entered (see Advisory Action mailed 10/8/03) because it did not comply with 37 CFR 1.121, specifically, the amended claims did not contain bracketing and underlining to identify changes to the claims. Claims 75 and 88-90 presented 10/24/03 are mis-identified as "NEW" and also do not contain bracketing and underlining to show the changes made. Therefore, claims 75 and 88-90 will be examined as they appear in the response filed 3/15/02. Any further amendments that do not comply with 37 CFR 1.121 will be considered non-responsive.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 75-82, 88-89 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by *Finer et al.* or *Bodner et al.*

Applicants, *Finer et al.* (U.S. Patent 5,686,279, issued 11/11/97, see whole document, particularly Columns 10-11, 17, Claims 1-11) and *Bodner et al.* (U.S. Patent 5,681,746, issued 10/28/97, see whole document, particularly Columns 11-22) all recite packaging cell lines for propagating retroviral vectors independent of helper viruses, said viral vectors comprising a nucleic acid component and two different non-nucleic acid components wherein said two different non-nucleic acid components can be two different envelope proteins (one having a tropism for the packaging cell (which can be a murine cell) and one having a tropism for a different target cell (which can be from a different species, i.e. human, and can be an epithelial cell or marrow cell or T-cell, etc.)), said nucleic acid and non-nucleic acid components being capable of forming a complex (i.e. a viral particle) and wherein said nucleic acid sequences encoding said components can be stably integrated into the cell genome or can be present extra chromosomally. The nucleic acid component of the vector can comprise sequences from two viruses that are native to the cell (i.e. encoding sequences for two different

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ecotropic or amphotropic envelopes, etc.). Therefore, Finer et al. and Bodner et al. teach the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 83, 85 rejected under 35 U.S.C. 103(a) as being unpatentable over Finer et al. in view of Respass et al.

Applicants claim a packaging cell comprising a viral vector which encodes an antisense RNA targeted against a mRNA coding for an undesirable protein in a target cell.

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Finer et al. is cited as in the above 35 USC 102(e) rejection of claims 75-82 and 88-90. Finer et al. does not teach expression of antisense sequences by viral vectors.

Respass et al. (U. S. Patent 6,013,517, issued 1/11/00, effective filing date 5/9/94, see whole document, particularly Columns 14-15, Claims 1, 8 and 11) recites the generation of packaging cell lines capable of generating retroviral vectors which are capable of expressing antisense RNAs complementary to undesirable mRNAs (i.e. mRNAs coding for cellular proteins required for cell growth in cancer cells) produced by target cells.

The ordinary skilled artisan, seeking to generate retroviral vector packaging cells capable of generating retroviral vectors capable of expressing an antisense sequence directed against the mRNA from an undesirable gene in a target cell, would have been motivated to combine the teachings of Finer et al. on the generation of retroviral packaging cells with the characteristics of claims 75-82 and 88-90 with the teachings of Respass et al. on the packaging cells which generate retroviral vectors capable of expressing antisense sequences targeted against mRNAs from undesirable genes in target cells because the expression of antisense sequences targeted against undesirable genes in target cells has been a well known technique to inhibit the growth of undesirable target cells or inhibit virus replication, etc. It would have been obvious for the ordinary skilled artisan to do this because use of viral (retroviral) vectors to deliver antisense sequences to target cells, in the context of treatment of diseases, was well known in the art (see Respass et al.) and was a standard use of retroviral vectors. Given the teachings of the cited prior art and the level of skill of the ordinary skilled

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artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 84 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Finer et al.* in view of *Bujard et al.*

Applicants claim a viral packaging cell line wherein the viral vector produced expresses a polypeptide of interest and an antisense RNA in a target cell.

Finer et al. is cited as in the above 35 USC 102(e) rejection. *Finer et al.* does not teach a packaging cell line producing a viral vector which expresses a polypeptide of interest and an antisense sequence in a target cell.

Bujard et al. (U.S. Patent 6,271,348, issued 8/7/01, effective filing date 6/7/95, see whole document, particularly Columns 18 and 21-22) recites the use of bi-directional promoters in viral vectors (which can be retroviral vectors) so that two gene products can be produced. The gene products can be two polypeptides of interest or two antisense sequences or a polypeptide and an antisense sequence.

The ordinary skilled artisan, seeking to generate a packaging cell line comprising a viral vector capable of expressing a polypeptide of interest and a antisense sequence in a target cell, would have been motivated to combine the teachings of *Finer et al.* with regard to the generation of packaging cell lines with the characteristics of claims 75-82 and 88-90 with the teachings of *Bujard et al.* on the use of viral vectors comprising bi-directional promoters for expression of multiple sequences encoding polypeptides

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and/or antisense sequences because the use of bi-directional promoters increases the versatility of viral vectors in that more than one sequence of interest can be expressed by a single vector. It would have been obvious for the ordinary skilled artisan to do this because being able to generate more versatile viral vectors capable of expressing two different sequences of interest would be desirable (See Bujard et al.). Given the teachings of the cited prior art and given the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 83, 85, 86-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Finer et al. in view of Dietz.

Applicants claim a packaging cell line comprising a viral vector which encodes an antisense RNA targeted against a mRNA coding for an undesirable protein in a target cell and wherein the antisense RNA can be a part of a chimeric RNA molecule that comprises sequences from small nuclear RNAs (for example, U1 snRNA).

Finer et al. is cited as in the above 35 USC 102(e) rejection of claims 75-82 and 88-90. Finer et al. does not teach expression of antisense sequences by viral vectors.

Dietz (U.S. Patent 5,814,500, issued 9/29/98, filed 10/31/96, see whole document, particularly Columns 2-3, 8 and Claims 1-11) recites the use of retroviral vectors to express antisense sequences targeted against undesirable target genes and wherein the antisense RNA is part of a chimeric RNA molecule that comprises sequences from snRNAs (such as U1 snRNA).

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The ordinary skilled artisan, seeking to develop packaging cell lines capable of generating retroviral vectors capable of expressing an antisense sequence or a chimeric antisense RNA molecule, would have been motivated to combine the teachings of Finer et al. on the generation of retroviral packaging cell lines with the characteristics of claims 75-82 and 88-90 with the teachings of Dietz concerning the use of retroviral vectors to express chimeric antisense sequences targeted against undesirable genes in target cells because the expression of antisense sequences targeted against undesirable genes was a well known technique in molecule biology and use of retroviral vectors to deliver chimeric RNAs to target cells was likewise known (Dietz). It would have been obvious for the ordinary skilled artisan to do this because delivery and expression of antisense sequences targeted against undesirable genes had been a well known (for almost two decades) technique in molecular biology. It would further have been obvious for the ordinary skilled artisan to select chimeric RNAs encoding antisense sequences and snRNAs because Dietz teaches that said chimeric RNAs make superior delivery vehicles for delivering the antisense sequences to the target cells. Given the teachings of the cited prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 77 and 87-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 77 is vague in that the tense of the word "comprise" should be singular (comprises) not plural.

Claim 87 is vague in that it refers to "The packaging cell line of any of claim 86..." because there is only one claim 86.

Claims 88-90 are vague in the recitation of the phrase "virus that is native to" the cell line or target cell. It is unclear if this phrase means that the virus naturally infects and replicates within the cell or that the virus can infect the cell but not replicate in the cell, or that the virus genome is present in the cell but it is not replicated, etc.

Claims 86-87 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Claims 86-87 have however been examined to the extent that is possible. A complete response to this Office Action must include correction of this defect.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571)

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272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
January 20, 2004


DAVID GUZO
PRIMARY EXAMINER